PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference A0272.12WO.1	**FOR FURTHER ACTION** See Form PCT/IPEA/416	
International application No. PCT/IB2004/000885	International filing date *(day/month/year)* 25.03.2004	Priority date *(day/month/year)* 01.04.2003
International Patent Classification (IPC) or national classification and IPC A61P31/04		
Applicant AVIP S.R.L		

1. This report is the International preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 3 sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (Indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the International application
- ☒ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
29.10.2004	08.07.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Stoltner, A Telephone No. +49 89 2399-8408

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/IB2004/000885

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-26 as originally filed

   Claims, Numbers

   1-15 received on 18.03.2005 with letter of 17.03.2005

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/IB2004/000885

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-15
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-15
Industrial applicability (IA)	Yes:	Claims	1-15
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

ad section V:

1). The subject-matter of the present application has been restricted to a composition comprising **Pediocin A or Pediocin A analogous molecules in combination** with at least one of their bacterial producer strains selected from:
Pediococcus pentosaceus FBB61, ATCC 43200;
Pediococcus pentosaceus FBB63;
Pediococcus pentosaceus L7230, ATCC 43201,
and its use as a medicament.

2). The present set of claims 1-15 finds basis on the description and the claims as previously on file (cf. letter of Applicant filed on 17/03/2005) and therefore complies with Arts. 6 and 19(2) PCT.

3a) The objective of the present application apparently resides in the provision of a combination of at least one bacteriocin with at least one producer strain in order to ameliorate the "digestive functionality and the gastrointestinal tract conditions" in monogastric organism species.

3b) Document D3, WO-A-9 729 645, provides a combination of Pediococcus pentosaceus with several pediocins for the treatment of bacterial infections in the stomach and the large and small intestinal tract (cf. abstract, page 1, paras. 1 and 2, page 3, last para., bridging with page 4, line 21).

Document D4, Microbiology, Soc. for Gen. Microbiology, Reading G, 140(part 4) april 1994, pp. 697-702, Piva et al., focuses on the food protecting role of **pediocin A, produced by Pediococcus pentosaceus FBB61**.

Document D5, Food Biotechnology, 6(2), 1992, pp. 153-174, Lewus et al., focuses in the bacteriocidal effects of pediocin A produced by Pediococcus pentosaceus, against Clostridium botulinum (cf. abstract, page 171, 3rd para.).

3c) The combination as presently depicted is nowhere explicitly described in the cited prior art documents. However, as a combination of Pediococcus pentosaceus with

several pediocins for the treatment of bacterial infections in the stomach and the large and small intestinal tract is derivable form D3, those skilled in the art receive the incentive to try, with reasonable expectation to succeed, further combinations of Pediococcus with pediocins including pediocin A in order to obtain similar or better therapeutic effects in the same field of therapy (treatment or improvement of gastrointestinal tract disorders). Therefore, and in the **absence of reliable data** proving for unexpected (synergistic) effects of the presently claimed specific **combination**, no inventive step can be recognised for the subject-matter of the present application.

ad section VIII:

1). The term "..for enhancing the sanitary conditions...in monogastric species.." in claim 4 lacks clarity and gives rise to so many possibilities rendering impossible to determine the exact scope of protection (Art. 6 PCT). Moreover, this term cannot be regarded as disease or disorder sufficiently defined for the treatment by a physician. This also applies to the term:

- "for developpong a better microbic intestinal balance.." (claim 5),
- "for reducing cresol production" (claim 6).

2). In a similar sence, the clarity objections raised in the former communication under section VIII (cf. IPER) have to be maintained.

AMENDED CLAIMS (Clean-Copy)

1. A composition comprising Pediocin A or Pediocin A analogous molecules in combination with at least one of their bacterial producer strains selected from the group consisting of:
Pediococcus pentosaceus FBB61, ATCC 43200;
Pediococcus pentosaceus FBB63;
Pediococcus pentosaceus L7230, ATCC 43201;
for use as a medicament.

2. A composition comprising at least one of the Pediocin A or Pediocin A analogous molecules bacterial producer strains as claimed in claim 1, for use as a medicament.

3. The composition according to claim 1 or 2, for use as a diet additive.

4. Use of the composition according to claim 1 or 2, for the preparation of a medicament, for enhancing the sanitary conditions of the intestine in monogastric species.

5. The use according to claim 4, for developping a better microbic intestinal balance.

6. The use according to claim 4, for reducing cresol production.

7. The use according to claim 4, for increasing polyamines production of bacterial origin into the intestinal lumen, said amines preferably being putrescine and spermidine.

8. The use according to claim 4, for increasing the epithelial surface of intestinal wall deputed to the absorbtion of nutrients.

9. The use according to claim 4, for increasing the length of villi in intestinal, proximal and medium jejunum.

10. The use according to claim 4, for increasing the thickness of brush border, constituted of microvilli at enterocytes luminal apex.

11. The use according to claim 4, for increasing the thickness of mucous tunica, both on a proximal and medium jejunum level.

12. The use according to claim 4, for incorporating said Pediocin A or Pediocin A analogous molecules as claimed in claim 1 into the mucous layer which covers the intestinal structures.

13. The use according to claim 4, for the prevention and prophylaxis of the intestinal pathologies by clostridia.

14. The use according to claim 13, for the prevention and prophylaxis of *Clostridium perfringens* infections.

15. The use according to anyone of claims 4 to 14, wherein said monogastric species are included among: human being, swines, rabbits, horses, poultry also wild, sheep, goats, felids, canids, ungulates, and non

functional ruminants.